

**AMENDMENTS TO THE SPECIFICATION:**

Please amend the specification as follows:

Please delete the paragraphs added to the beginning of the specification by preliminary amendment on March 9, 2001. Please replace the paragraph beginning at page 1, line 1, of the specification as filed, with the following amended paragraph:

This application is a continuation of USSN 08/925,779, filed September 9, 1997 (U.S. Patent No. 6,245,889), which is a continuation of USSN 07/721,847, filed June 14, 1991 (U.S. Patent No. 6,150,328), which is a continuation-in-part of U.S. Serial Nos. 07/493,272, filed March 14, 1990 (abandoned) (which is a CIP of 07/406,217, filed September 12, 1989 (abandoned)); 378,537 filed July 11, 1989; and 655,579, filed February 14, 1991 (U.S. Patent No. 5,618,924), which is a divisional of 07/179,100, filed April 8, 1988 (now U.S. Patent No. 5,013,649) which is a continuation-in-part of 07/028,280, filed March 20, 1987 now abandoned; 943,532, filed December 17, 1986 now abandoned; and 880,776, filed July 1, 1986 now abandoned.

Please replace the paragraph beginning at page 23, line 19, with the following amended paragraph:

Full length human BMP-2 cDNA clones are obtained in the following manner. The 1.5 kb insert of one of the BMP-4 subclones (II-10-1) is isolated and radioactively labeled by nick-translation. One set of the nitrocellulose replicas of the U-2 OS cDNA library screened above (50 filters, corresponding to 1,000,000 recombinant bacteriophage) are rehybridized with this probe under stringent conditions (hybridization at 65° in 0.2 X SSC, 0.1% SDS). All recombinants which hybridize to the bone genomic probe which do not hybridize to the BMP-4 probe are picked and plaque purified (10

FINNEGAN  
HENDERSON  
FARABOW  
GARRETT &  
DUNNER LLP

1300 I Street, NW  
Washington, DC 20005  
202.408.4000  
Fax 202.408.4400  
www.finnegan.com

recombinants). Plate stocks are made and small scale bacteriophage DNA preparations made. After subcloning into M13, sequence analysis indicates that 4 of these represent clones which overlap the original BMP-2 clone. ~~One~~ Two of these, lambda U2OS-39 and U2OS-3, was were deposited with the ATCC (10801 University Boulevard, Manassas, VA, 20110-2209), under the Budapest Treaty, on June 16, 1987 under accession number 40345 and 40342, respectively. The DNA sequence (SEQ ID NO: 3) (compiled from lambda U2OS-39 and several other hBMP-2 cDNA recombinants) and derived amino acid sequence (SEQ ID NO: 4) are shown below in Figure 2. Lambda U2OS-39 is expected to contain all the nucleotide sequence necessary to encode the entire human counterpart of the protein BMP-2 encoded by the bovine gene segment whose partial sequence is presented in Figure 1. The BMP-2 protein encoded by the DNA sequence of Figure 2 is contemplated to contain the 97 amino acid sequence from amino acid #299 to #396 or a sequence substantially homologous thereto. This human cDNA hBMP-2 contains an open reading frame of 1188 bp, encoding a protein of 396 amino acids. The protein is preceded by a 5' untranslated region of 342 bp with stop codons in all frames. The 13 bp region preceding this 5' untranslated region represents a linker used in the cDNA cloning procedure. This protein of 396 amino acids has a molecular weight of 45kd based on this amino acid sequence. It is contemplated that this sequence represents the primary translation product. It is further contemplated that BMP-2 may correspond to the approximately 18 - 20 kd subunit of Example IIC. The sequence corresponding to the sequence tryptic Fragment 3 of Example IV is underlined in Figure 2. The "pre" portion of the human BMP-2 protein is contemplated to comprise amino acid #1 to amino acid

FINNEGAN  
HENDERSON  
FARABOW  
GARRETT &  
DUNNER LLP

1300 I Street, NW  
Washington, DC 20005  
202.408.4000  
Fax 202.408.4400  
www.finnegan.com

#23 as shown in Figure 2. The "pro" portion is contemplated to comprise amino acid #24 to amino acid #282 of Figure 2 (SEQ ID NO: 4). The mature portion is contemplated to comprise amino acid #283 (Gln, Ala, Lys...) to #396 (Arg) of Figure 2.

FINNEGAN  
HENDERSON  
FARABOW  
GARRETT &  
DUNNER <sup>LLP</sup>

1300 I Street, NW  
Washington, DC 20005  
202.408.4000  
Fax 202.408.4400  
[www.finnegan.com](http://www.finnegan.com)